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SPERMATOGENIC STAGE SPECIFICITY OF ACRYLAMIDE-INDUCED CHROMOSOME ABERRATIONS DETECTED IN MOUSE ZYGOTES USING FISH CHROMOSOME PAINTING. F. Marchetti, X. Lowe, A. Wyrobek. Biology and Biotechnology Research Program, Lawrence Livermore National Laboratory, Livermore, CA.

The time course of the induction and transmission of chromosome aberrations in germ cells of males treated with acrylamide (AA) was investigated in mouse zygote metaphases. Male mice treated with 5 daily injections of 50 mg/kg AA were mated with untreated females at intervals corresponding to treatment of epididymal sperm (2.5 days after the last injection), testicular sperm (6.5 days), late spermatids (9.5 days), mid-spermatids (12.5 days), spermatocytes (27.5 days) and spermatogonia (48.5 days). Zygote metaphases were scored for the induction of structural aberrations after conventional staining (DAPI analysis) and after chromosome painting (PAINT analysis) using four biotin-labeled probes specific for chromosomes 1, 2, 3, and X, plus a digoxigenin-labeled probe specific for chromosome Y. After DAPI analysis, the frequencies of zygotes with structural aberrations at the respective mating intervals were: 55.2% (48/87), 75.8% (75/99), 47.6% (49/103), 7.5% (7/93), 0% (0/52) and 0% (0/81). The same metaphases were also scored by PAINT analysis registering only those aberrations that involved painted chromosomes. Using cell-equivalents (ce) to account for the fraction of the genome painted, the frequencies of zygotes with structural aberrations at the respective mating intervals were: 65.9% (23/34.9 ce), 160.7% (36/22.4 ce), 75.7% (31/40.9 ce), 10.8% (4/37.1 ce), 0% (0/20.6 ce) and 0% (0/32.2 ce). The frequencies of aberrant zygotes detected by PAINT analysis were consistently higher than those detected by DAPI analysis. This was due to the ability of PAINT analysis to detect reciprocal translocations and insertions. Our findings show that the clastogenic effects of AA on male germ cells are limited to postmeiotic stages of spermatogenesis, and that PAINT analysis of mouse zygotes is a powerful tool for the investigation of the effects of parental exposure to mutagens on the offspring. (Work performed under the auspices of the U.S. DOE by the Lawrence Livermore National Laboratory under contract W-7405-ENG-48 with support from NIEHS Y01-ES-10203-00)